REMARKS

Reconsideration is requested.

Claim 68 has been canceled, without prejudice.

Claims 69-70 73, 74, 76, 87-90, 95-97 and 102 are pending. Claim 95 is indicated as being free of the art. The Examiner's indication that claims 96 and 97 contain allowable subject matter is acknowledged, with appreciation. The allowance of claim 102 is requested as the claim has not been rejected and only objected-to on page 1 of the Office Action dated June 8, 2006, without further comment or explanation.

The Office Action of June 8, 2006 is understood to contain the following rejections of the noted claims:

(1) Claims 68-69, 73, 87 and 88 have been rejected as allegedly being anticipated by Ralston (WO 92/08734A1),

(2) Claims 76 and 87 have been rejected as allegedly being anticipated by Hsu (Hepatology, May 1993, Vol. 17, No. 5, pp 763-771),

(3) Claims 68-70, 73, 87, 88 and 102 have been rejected as allegedly being anticipated by Selby (U.S. Patent No. 6,121,020),

(4) Claims 68, 69, 73, 87 and 88 have been rejected as allegedly being anticipated by Ralston (U.S. Patent No. 5,942,234), and

(5) Claims 68-70, 73, 74, 87-90 and 102 have been rejected as allegedly having been obvious in view of the combination of Selby, Tartaglia (Virology 1992, Vol. 188 (1), pp 217-232), Sutter (PNAS, 1992, Vol. 89, pp 10847-10851) and Vanderbroeck (European Journal of Biochemistry 1993, Vol. 217, pp 45-52).

The Examiner is requested to advise the undersigned in the event any further rejection or objection to the claims and/or specification are contained in the Office Action of June 8, 2006.

Attached is a copy of the applicants priority document EP 94870132.1, filed July 29, 1994. A certified copy of the same will be filed under separate cover. Support for the claimed invention can be found, for example, at page 2, lines 13-15; page 13, line 5 to page 14 ,line 15; and Example 1-2 of the priority document.

The above-listed rejections (3) and (5), based on Selby, are obviated by the attached as Selby, which claims an earliest filing date in the U.S. as July 29, 1994, is not citable prior art to against the applicants claims. Withdrawal of the Section 102 rejection of claims 68-70, 73, 87, 88 and 102 over Selby (U.S. Patent No. 6,121,020) is requested. Withdrawal of the Section 103 rejection of claims 68-70, 73, 74, 87-90 and 102 over the combination of Selby, Tartaglia (Virology 1992, Vol. 188 (1), pp 217-232), Sutter (PNAS, 1992, Vol. 89, pp 10847-10851) and Vanderbroeck (European Journal of Biochemistry 1993, Vol. 217, pp 45-52) is requested.

The Section 102 rejection of claims 68-69, 73, 87 and 88 over Ralston (WO 92/08734A1) is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing comments.

A *prima facie* case of anticipation is understood to require that a reference literally or inherently teaches each and every aspect of a claimed invention.

Ralston fails to teach each and every aspect of the claimed invention.

Claim 69 requires, for example, the following:

> with said nucleotide sequence being characterised further in that it encodes a single HCV E1 protein starting in the region between amino acid positions 117 and 192 and ending in the region between amino acid positions 285 and 326.

The Examiner states the following in the paragraph spanning pages 2-3 of the Office Action dated June 8, 2006:

> "The full length HCV E1 ranges from amino acid residue 192-384. If the deleted region is located in the range somewhere in 260-290 and 330-380, but before the 285 or 400, the HCV E1 polypeptide will start before the region 170 or 190 and end at a position within the region between the amino acid residues 260-290 or 330-380."

The Examiner appears to be relying on the following disclosure of Ralston (spanning pages 10-11 of Ralston (emphasis added)):

> "Additionally, it may be advantageous to express a truncated form of the envelope protein. Both E1 and E2 appear to have a highly hydrophobic domain, which apparently anchors the protein within the endoplasmic reticulum and prevents efficient release. Thus, one may wish to delete portions of the sequence found in one or more of the regions aa170-190, aa260-290 or aa330-380 of E1 (numbering from the beginning of the polyprotein), and aa660-830 of E2 (see for example Figure 20-1 of EP 388,232). It is likely that at least one of these hydrophobic domains forms a transmembrane region which is not essential for antigenicity of the protein, and which may thus be deleted without detrimental effect. The best region to delete may be determined by conducting a small number of deletion experiments within the skill of one of the ordinary practitioner. Deletion of the hydrophobic 3' end of E2 results in secretion of a portion of the E2 expressed, with sialyation of the secreted protein."

One of ordinary skill in the art would not understand the above to be a specific teaching to produce a recombinant vaccinia vector of the claims or even a nucleic sequence of the claims which encodes a single HCV E1 protein starting in the region

between amino acid position 117 and 192 and ending in the region between amino acid positions 285 and 326.

At best, one of ordinary skill in the art would interpret the quoted passage, which is apparently relied on by the Examiner, as teaching an HCV sequence containing at least E1 and E2 sequences where one or more of the recited hydrophobic regions (i.e., "portions of the [HCV] sequence found in one or more of the regions") is deleted.

The reference fails to specifically teach each and every aspect of the claimed invention.

Regarding the method for expression of the HCV E1 proteins, Ralston et al. teach to express the HCV E1 protein as a large polyprotein (first 850-900 amino acids of the HCV polyprotein), that can be further post-translationally processed in a eukaryotic host cell (page 9, lines 20-23). Ralston only generally mentions that

> "one may truncate the 5' end of the coding region to reduce the amount of C protein produced" (page 9, lines 24-25),

without providing further specifics. No further information or description is provided regarding truncating the 3' end of the coding region. As such, a recombinant vaccinia vector encoding a HCV polyprotein ending around aa 850-900 is clearly different from the recombinant vaccinia vectors of the present invention, which will express the HCV E1 protein starting in the region between aa 117-192 and ending in the region between aa 285 and 326.

Further, Example 1 of Ralston (page 17-19) is understood to describe, at best, the vaccinia vectors that were constructed:

One construct contains a HCV nucleotide sequence encoding the 5' end of the HCV polyprotein from amino acid 1 to amino acid 906, beginning at nucleotide -63 relative to amino acid 1

A second construct contains a HCV nucleotide sequence encoding the 5' end of the HCV polyprotein from amino acid 1 to amino acid 906, beginning at nucleotide -6 relative to amino acid 1

A third construct contains a HCV nucleotide sequence encoding the 5' end of the HCV polyprotein from amino acid 1 to amino acid 364

A fourth construct contains a HCV nucleotide sequence encoding part of the HCV polyprotein from amino acid 364 to amino acid 906

A fifth construct contains a HCV nucleotide sequence encoding part of the HCV polyprotein from amino acid 406 to amino acid 661

These vaccinia constructs do not literally describe the claimed invention. The constructs of Ralston are clearly different from the vaccinia constructs claimed in the present invention, which contain a nucleotide sequence encoding a single HCV E1 protein starting in the region between amino acid 117 and 192 and ending in the region between amino acid 285 and 400.

The claims are submitted to be patentable over Ralston and withdrawal of the Section 102 rejection of claims 68-69, 73, 87 and 88 over the same is requested.

The Section 102 rejection of claims 76 and 87 over Hsu (Hepatology, May 1993, Vol. 17, No. 5, pp 763-771) is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing comments.

After careful reading of the cited document of Hsu et al., the applicants are not able to locate in the text of Hsu et al the teaching described by the Examiner on page 3 of the Office Action dated June 8, 2006. Clarification is requested in the event the rejection is maintained.

Specifically, the Examiner states (emphasis added) that the reference

> "discloses a recombinant baculovirus expression vector in particular HCV-Bac 3, encoding nucleic acid sequence that encodes the HCV envelope protein E1 protein ranging from nucleic acid base 400 to 950 or amino acid residues 133 to 316, **wherein the glycosylation site(s) at the position 325 is removed inherently at the nucleic acid level**."

The Examiner is requested to specifically indicate where the reference describes the same in the event the rejection is maintained.

Further explanation of the relevance of the Examiner's comment is also requested in the event the rejection is maintained. The applicants believe that recombinant baculovirus HCV-Bac 3 is constructed to allow expression of an HCV E1 protein starting at amino acid 133 and ending at amino acid 316. As such, the glycosylation site at amino acid position 325 is not originally present within said E1 protein. This is completely different from the requirements of the rejected claims 76 and 87 which provide a recombinant vector construct comprising a nucleic acid sequence to allow expression of an HCV E1 protein, wherein at least one glycosylation site present in said E1 has been removed at the nucleic acid level. More specifically, claim 76 includes an HCV E1 expression vector with E1 starting at amino acid 133 and ending at amino acid 316, **and** in which additionally a glycosylation site is removed. Hsu et al. disclose an HCV E1 expression vector with E1 starting at amino acid 133 and ending at

amino acid 316. Hsu et al. does not disclose removal of a glycosylation site in this HCV E1. Thus, claims 76 and 87 are submitted to be patentable over Hsu et al and withdrawal of the Section 102 rejection is requested.

The Section 102 rejection of claims 68, 69, 73, 87 and 88 over Ralston (U.S. Patent No. 5,942,234) is traversed. Reconsideration and withdrawal of the rejection are requested in view of the above comments relating to the patentability of the claims over the related Ralston (WO 92/08734). The Examiner's reliance on and comments regarding U.S. Patent No. 5,942,234 and WO 92/08734 appear to be similar and the disclosure of the documents appear similar. The claims are patentable over U.S. Patent No. 5,942,234 for the reasons noted above with regard to WO 92/08734. Withdrawal of the Section 102 rejection of claims 68, 69, 73, 87 and 88 over Ralston (U.S. Patent No. 5,942,234) is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned in the event anything further is required.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: /B. J. Sadoff/
B. J. Sadoff
Reg. No. 36,663

BJS:
901 North Glebe Road, 11th Floor
Arlington, VA 22203-1808
Telephone: (703) 816-4000
Facsimile: (703) 816-4100